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Folates and Methotrexate

5-formyl tetrahydrofolate (leucovorin)

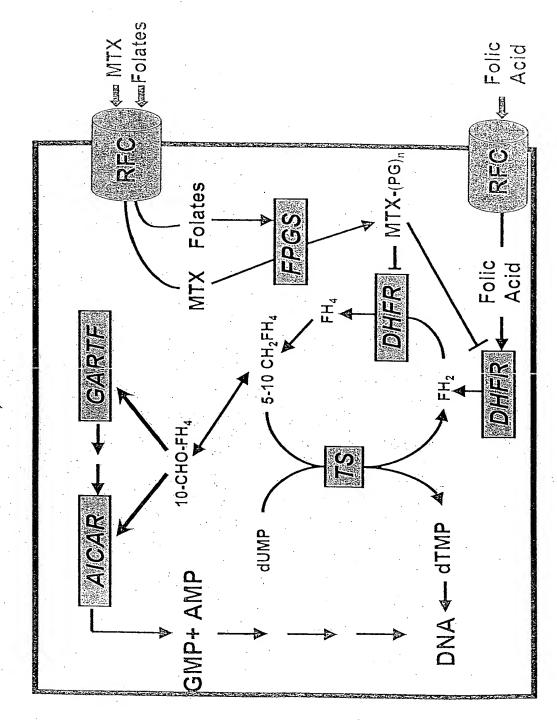
Folic Acid

$$\begin{array}{c|c} CH_{3} & C \\ NH_{2} & N \\ \hline \\ N & N \\ \end{array}$$

$$\begin{array}{c|c} CH_{3} & C \\ \hline \\ CH_{2} & N \\ \hline \\ CH_{2} & N \\ \end{array}$$

$$\begin{array}{c|c} CH_{3} & C \\ \hline \\ CH_{2} & CH_{3} \\ \hline \\ COOH \\ \end{array}$$

Methotrexate (MTX)



4.5.7

Protocol for Genomic PCR-SSCP Analysis of Human RFC

Tumor Specimens; Tumor cell lines; Blood

Isolate Genomic DNA

Genomic PCR

SSCP Analysis & Detection of Electrophoretic Mobility Change

T/A Cloning and Sequencing

Direct DNA Sequencing

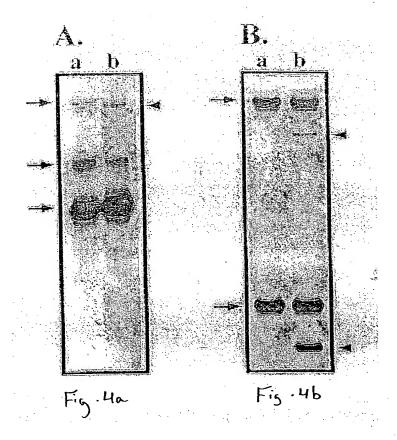
Identify the Genetic Alteration(s)

Point mutation(s) and/or Polymorphism

In-Vitro Mutagenesis

Transfect the Mutated RFC cDNA into Transport Null Cells

Measure MTX/folate Transport



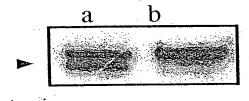
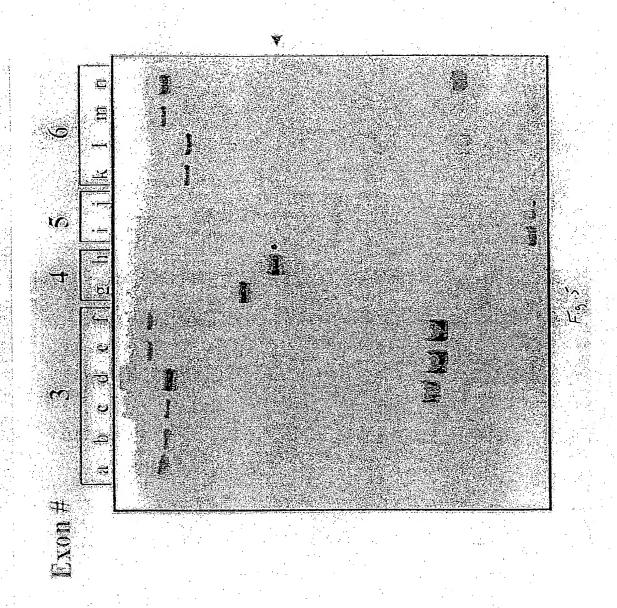


Fig. 4c



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